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Infliximab in recalcitrant generalized pustular arthropatic psoriasis

Generalized pustular psoriasis is an unstable inflammatory type of psoriasis, with widespread areas of erythema and sterile pustules, associated with fever and systemic symptoms. Infliximab is a monoclonal antibody with anti-TNFα activity, approved for use in psoriasis. We describe a male patient with a long history of stable arthropathic psoriasis, hospitalized with a generalized pustular psoriasis and acute exacerbation of articular complaints. The disease was resistant to multiple therapies (acitretin, methotrexate and corticosteroids), so the patient was started on infliximab, with a very rapid response of both cutaneous and articular symptoms. He had complete clearing of lesions at week 12, and marked improvement of the articular symptoms. No recurrence occurred at 8 months of follow-up with infliximab every 8 weeks. Infliximab had an extremely rapid therapeutic action response on a recalcitrant generalized pustular psoriasis. The articular response was also excellent, with significant improvement of quality of life.

Key words: anti-TNF-alpha, arthropatic, biologics, infliximab, pustular psoriasis

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Generalized pustular psoriasis (Von Zumbusch type) is an unstable inflammatory type of psoriasis, with widespread areas of erythema and sterile pustules, associated with fever and systemic symptoms [1]. In this form of psoriasis, infiltration of the skin with neutrophils plays an important role, leading to the characteristic sterile pustules [2]. Infliximab is a monoclonal antibody with activity against tumour necrosis factor-α (TNF-α), approved for use in psoriasis [3]. The very rapid onset of action and reported efficacy makes it an appealing option for the treatment of generalized pustular psoriasis [4].

Case report

A 59-year-old male patient, with a 24-year history of plaque psoriasis with moderate articular involvement, was hospitalized with a severe generalized pustular eruption. The disease had been stable and localized, with moderate articular complaints, mostly axial. Betamethasone cream, calcipotriol ointment and naproxen were the only previous medication, along with chronic anti-hypertensive therapy (indapamide, losartan and perindopril).
He developed an inflammatory flare-up of the disease, with erythematous plaques on the upper trunk, which rapidly generalized, affecting 90% of the body surface *(figure 1)*. Small non-follicular pustules developed over these inflammatory lesions and fever (38 °C), malaise, and severe worsening of articular complaints occurred simultaneously, causing notable difficulty with mobilization.
The patient denied previous use of systemic corticosteroids or any new medication recently. Infectious and metabolic triggers were ruled out by clinical and analytical evaluation, in particular hypocalcemia, streptococcal or human immunodeficiency virus infection. On admission, the patient had a white blood cell count of $13.4 \times 10^3/\mu L$ with 91% neutrophils, erythrocyte sedimentation rate of 58 mm and C reactive protein of 23.1 mg/dL.
Treatment was started with methotrexate (15 mg/weekly PO) and acitretin (35 mg/d), but new pustules and very severe articular pain continued after three weeks of treatment. As uncontrolled hypertension precluded the use of cyclosporine, systemic corticosteroids (1 mg/kg/d) were added, while waiting for the full therapeutic effect of methotrexate and acitretin. There was a rapid resolution of the pustular eruption, fever and improvement of articular complaints, and slow tapering of corticosteroids was started (10% weekly dose reduction over 5 weeks). When the dose reached 0.5 mg/kg/d, new pustules appeared together with worsening of articular complaints. The corticosteroids were stopped, and after exclusion of latent tuberculous infection, infliximab was started at 5 mg/kg IV (weeks 0, 2 and 6, and then every 8 weeks) and both methotrexate and acitretin were maintained. There was an extremely rapid response, noticeable from the second day, with complete clearance of the pustular eruption at the end of the first week *(figure 2)*. There was also an improvement in both articular pain and mobility, and methotrexate and acitretin were stopped at the second infliximab infusion. Complete clearance of cutaneous lesions was achieved at 12 weeks, with no significant side effects reported. No relapse was noted at 26 weeks follow-up, with special emphasis on the continued articular improvement.

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Figure 1. Generalized pustular psoriasis. **A**) Multiple active lesions despite combination therapy; **B**) Rapid improvement after one week of the first infliximab infusion; **C**) Complete resolution after 3 infliximab infusions (12 weeks).

Discussion

Generalized pustular psoriasis (GPP) is a serious dermatological disease, which can result in significant morbidity and even mortality [5]. The disease is characterized by fever, systemic symptoms and generalized pustule formation on the skin [1].

GPP frequently occurs as an inflammatory flare-up of a stable psoriasis, often associated with the use of systemic corticosteroids, and more rarely topical corticosteroids [6, 7]. Many other triggers have been described, like pregnancy, hypocalcemia, infections and sudden withdrawal of anti-psoriatic therapy [8-10]. No infectious, metabolic or drug-induced trigger was identified in our patient.

Acitretin has good efficacy in pustular psoriasis, with inhibition of neutrophil migration and activation [11]. We combined acitretin and methotrexate for our patient in order to target both the skin and articular involvement [12]. Systemic corticosteroids were used to rapidly control the inflammatory flare of the disease, while waiting for the full therapeutic effect of methothrexate.

Infliximab has shown good efficacy and very rapid onset of action for plaque psoriasis and psoriatic arthritis, with a beneficial impact on quality of life and work productivity [3, 13-15]. The experience with infliximab in clinical practice has been expanding, although few reports have been published on its use in GPP [16-19]. Even in severe recalcitrant cases, infliximab has been shown to be highly effective in rapidly controlling the disease [5, 20-22]. By inhibiting TNF-α, it appears to downregulate neutrophil-attractant chemokines which play a relevant role on the pathogenesis of the disease, such as interleukin-8 (IL-8),

Figure 2. Generalized pustular psoriasis and infliximab therapy: **A**) Pre-treatment; **B**) After one week; **C**) After 12 weeks.

growth-related oncogene (Gro-α) and monocyte chemoattractant protein (MCP-1) [22].

Our patient had an excellent response to infliximab, with improvement noticeable from the second day. Complete clearance of the lesions occurred at week 12, after only three infusions. This very rapid onset of action has already been described [20, 21], making it a very attractive therapy for inpatients, by rapidly and efficiently controlling the disease and allowing early discharge from hospital [4]. ■

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